

Amendments to the Specification

Page 7, paragraph beginning on line 13 is amended as follows:

Instead to the ζ -chain, the fusion receptors of the invention may include other cytoplasmic domains. For example, CD28 can be used as the cytoplasmic domain to enhance T-cell activation, survival and proliferation. A preferred CD28 moiety is one which spans amino acids encoded by bases 336 to 663 of CD28 cDNA, in which case no connector is needed to retain function. PSMA-fusion receptors incorporating 41BB as the cytoplasmic domain have also been prepared. Both the PSMA-CD28 and the PSMA-41BB fusion receptors have been made and tested in the same experimental model used with the PSMA- ζ chain fusion receptor. In both cases, sustained proliferation was observed in both human CD4⁺ and CD8⁺ primary T cells (PBL) in the presence of PSMA⁺ cells, with more sustained proliferation being provided by the PSMA-41BB fusion receptor. High production of IFN- γ and IL-2 was observed, for PSMA-41BB and PSMA-CD28 transduced, respectively. In each of the experiments performed, an external signal to complement the signaling of the fusion receptor was used. However, transfection of the PBL with fusion receptors encoding both the ζ -chain and either CD28 or 41BB or a comparable costimulatory molecule would eliminate this requirement. Thus, for example, PBL transduced with both the PSMA- ζ chain fusion receptor and either a PSMA-fusion receptor with a secondary signaling moiety would provide therapeutic efficacy for *in vivo* use.

Page 10, paragraph beginning on line 18 is amended as follows:

Next, an oligonucleotide encoding the human CD8 leader sequence was cloned to the 5'-end of the V_H gene, and the 3'-end of the V_H gene was cloned to an oligonucleotide encoding a (gly-ser)₂ linker (Seq ID No.: 9) followed by the V_L gene, creating the PSMA-specific scFv. The scFv was then cloned to the CD8 hinge and transmembrane domains, followed by the T cell receptor ζ -chain cytoplasmic domain to create Pz-1, a PSMA-specific scFv/ ζ -chain chimeric T-cell receptor. The Pz-1 fusion gene was then cloned into the SFG retroviral vector (Riviere et al, *supra*) as illustrated in Fig. 1.

Page 15, the paragraph beginning on line 4 is amended as follows:

A segment of the human CD28 cDNA that encodes part of the extracellular, the transmembrane, and the cytoplasmic domains (~~amino acids~~ nucleotides 336 to 663) was amplified by PCR from the plasmid pbsCD28, using the upstream primer

5'GCGGCCGCAATTGAAGTTATGTATCCT

SEQ ID No. 7

Appln No.: 09/786,502
Amendment Dated: December 15, 2005
Reply to Office Action of September 21, 2005

and the downstream primer

5'TCGAGGATCTTGTTCAGGAGCGATAGGCTGC

SEQ ID No. 8.

These primers contain NotI and BamHI sites respectively for the insertion of the PCR product in the retroviral Vector SFG. Following digestion of the purified PCR product with NotI and BamHI, the CD28 fragment was ligated into the NotI and BamHI sites of the retroviral vector SFG, containing the CD8 α leader sequence, followed by the single chain gene, encoding the V_H and V_L domains of the PSMA-specific antibody